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ABSTRACT

This paper outlines research designed to establish dietary correlates of malnutrition, and questions the common assumption that high protein foods should be used as dietary supplements in humans. Because thorough investigation of dietary needs in children is ethically unfeasible, squirrel monkeys were used in the research to study the biological and mental effects and the behavioral correlates of deficiency disease. Infant squirrel monkeys were taken from their mothers after birth and fed a low-protein diet from 2 weeks to 8 weeks of age. Group rearing conditions were provided by satellite cage arrangements for every four animals. The members of these social groups were allowed to interact for four hours a day. All animals were given normal diets at the age of 8 weeks. (GO)

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OVERALL RATIONALE AND DESIGN OF STUDY

D. Mark Hegsted

My primary function today is to describe the overall design of the investigations. My colleagues will report the experimental findings. However, I do wish to say a few words about the general problem of protein-calorie malnutrition. It is generally agreed that this is the most important nutritional deficiency disease in the world and is a major cause of the high mortality in infants and young children--sometimes reaching 40 to 50% of the births--in the developing parts of the world.

A primary aim of the nutritional investigations is to characterize protein and calorie deficiency, independently, and the effects of varying degrees of combined protein and calorie deficiency. We are occasionally asked why we should do this. Is it not enough to know that children are malnourished and, if they are, why do we not simply feed them? Feeding people anywhere in the world is difficult and in many places may be impossible. We are dealing not only with money and sources of food but the development of an effective delivery system which will reach those in need. Effective systems have not yet been developed.

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The development of appropriate systems depends upon a correct diagnosis of the problem. The position taken by many agencies and scientists during the past 25 years is that protein deficiency is the primary problem. Although I cannot discuss the evidence in detail, there is now great doubt that this is a correct conclusion. We should note that infants do very well upon a food which is relatively low in protein content--breast milk. This contains a lower protein concentration than most diets consumed by adults. They do not require "high protein diets."

The infant monkey appears to be a very satisfactory model primarily because the growth rate is relatively slow, as it is in man. This contrasts with the situation in most experimental and farm animals which grow rapidly and in which the growth requirements dominate the nutritional needs. In such animals the growing animal does indeed require high protein diets. Extrapolation from such studies to man have contributed to the misconceptions about the protein needs of infants and children.

The extremes of protein-calorie malnutrition are kwashiorkor--thought to represent "protein" deficiency--and marasmus--thought to represent severe calorie deficiency or partial starvation. The antecedants of these diseases, however, are almost never known. Such data as are available do not necessarily indicate that those who develop kwashiorkor usually consume less protein than those who develop marasmus.

In infant monkeys both calorie and protein deficiency produce a marasmic condition. Some animals which are fed low protein diets eventually develop what appears to be full-blown kwashiorkor, i.e., a disease characterized by low plasma albumin, edema, skin lesions and fatty liver. The point we would make is that appearance of the animals is not a discriminating method for distinguishing between calorie and protein deficiency and there is reason to believe that this is also true of children.

Kwashiorkor, with all of the hallmarks of protein deficiency, appears to be an acute disease possibly superimposed upon an infant who is probably already marginally deficient in various nutrients. Kwashiorkor is usually associated with infections and diarrhea. When the infant becomes ill his appetite fails; his diet is often changed to a less nutritious one--

a thin gruel which may be very low in protein content; he suffers the catabolic effects of the illness and loses nutrients because of the diarrhea, etc. Thus, the fact that he develops protein deficiency may or may not have direct relationships to the nutrient content of his "usual diet" and modification of his usual diet may not be effective in preventing the development of the disease.

If protein deficiency is the primary cause of malnutrition in many parts of the world, the strategy for dealing with malnutrition may be quite different than if it is due to other causes. Although it is not easily done, protein sources can be added to the food supply. This, however, is an expensive proposition and unless it is effective this additional burden should not be imposed upon an already expensive and limited food supply.

It must be agreed that easily available and suitable foods to feed young infants and children are not available in many parts of the world. Whether such foods need to be "high protein foods" is however questionable. Many attempts have been and are being made to prepare such foods around the world. The emphasis upon protein may have inhibited the development of more effective solutions at lower cost.

It is obvious that many of the problems posed cannot, for ethical reasons, be thoroughly investigated with infants and children. Appropriate animal models are needed. While our nutritional group is primarily interested in defining nutritional needs and characterizing the biological effects of deficiency disease, we thought we could not in good conscience ignore the possible effects of malnutrition upon behavior and mental development which have been widely discussed in both the public and scientific press. The kinds of experiments we are discussing are

expensive and probably will not be extensively duplicated. We welcomed the collaboration of a psychological team. The report today is concerned with a study of protein deficiency. Future studies will be aimed at calorie deficiency and combined protein and calorie limitation. Clearly, if nutritional deficiencies have specific effects upon behavior and development, the combined efforts of nutritionists, biochemists, psychologists, and other kinds of expertise will be required.

The use of a primate model permits the establishment of nutrition and social environment as separate and independent variables and the separation of contemporaneous effects during periods of deprivation from the residual effects following the introduction of rehabilitative regimes. The work to be reported represents a full year study following a number of pilot efforts. The studies have been done with squirrel monkeys; parallel work on the cebus monkeys, another New World species, is in progress. As indicated, other types of nutritional deprivation and social conditions will be explored in the future.

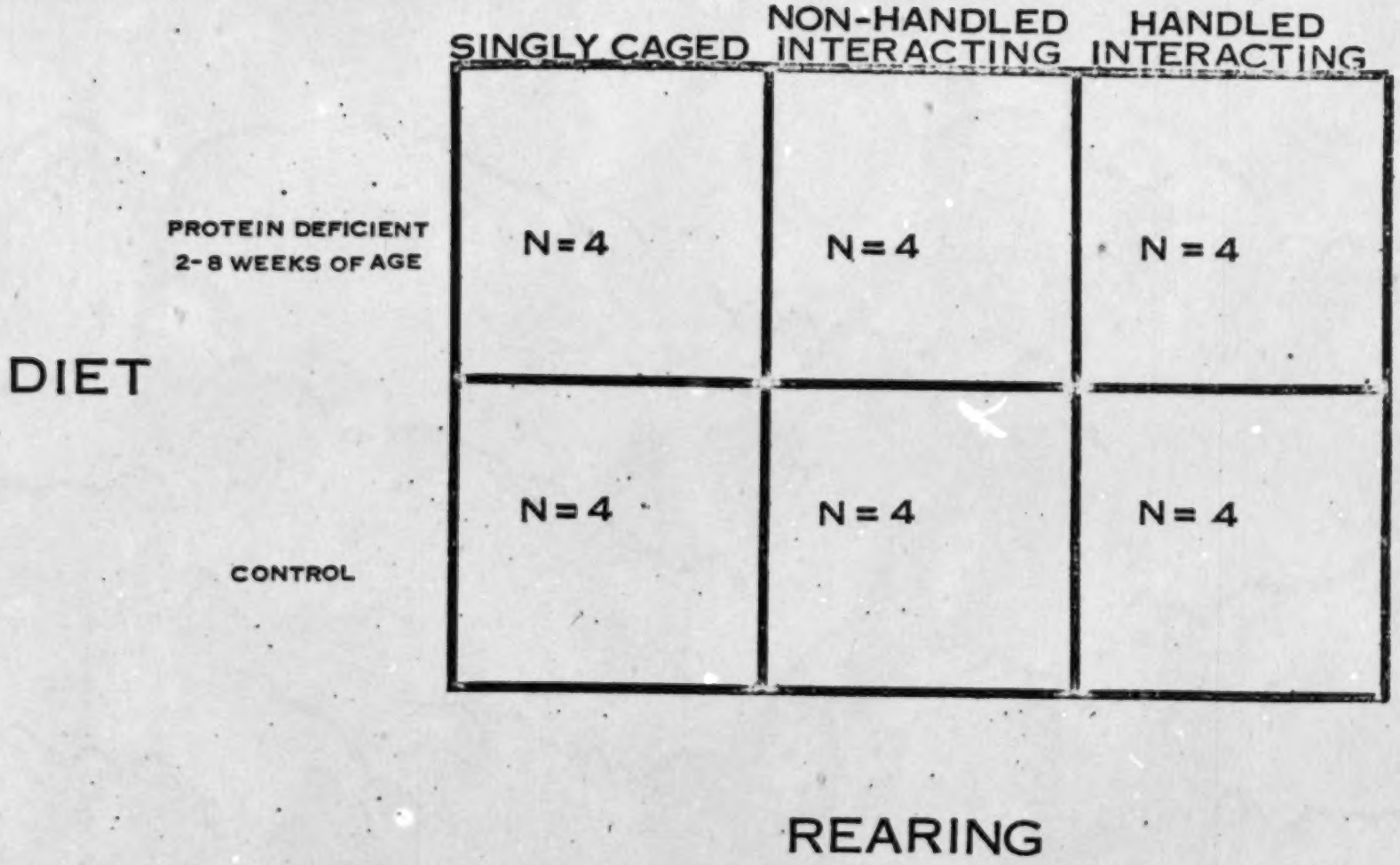
The basic experimental design is indicated in the first slide.

Babies are born in the colony of well-nourished squirrel monkeys maintained in the laboratory and immediately removed from their mothers as soon as discovered--always within 24 hours. For the next two weeks they were handfed in a warming crib with a dietary formula of demonstrated adequacy for physical growth. Those animals to be nutritionally deprived were fed a low protein diet *ad libitum*, 2½ to 4½ of the calories as protein, the level of protein being individually adjusted for each animal so that his weight remained constant or grew at a very slow rate. Deprivation began at 2 weeks of age and continued until 8 weeks of age--a deprivation period of

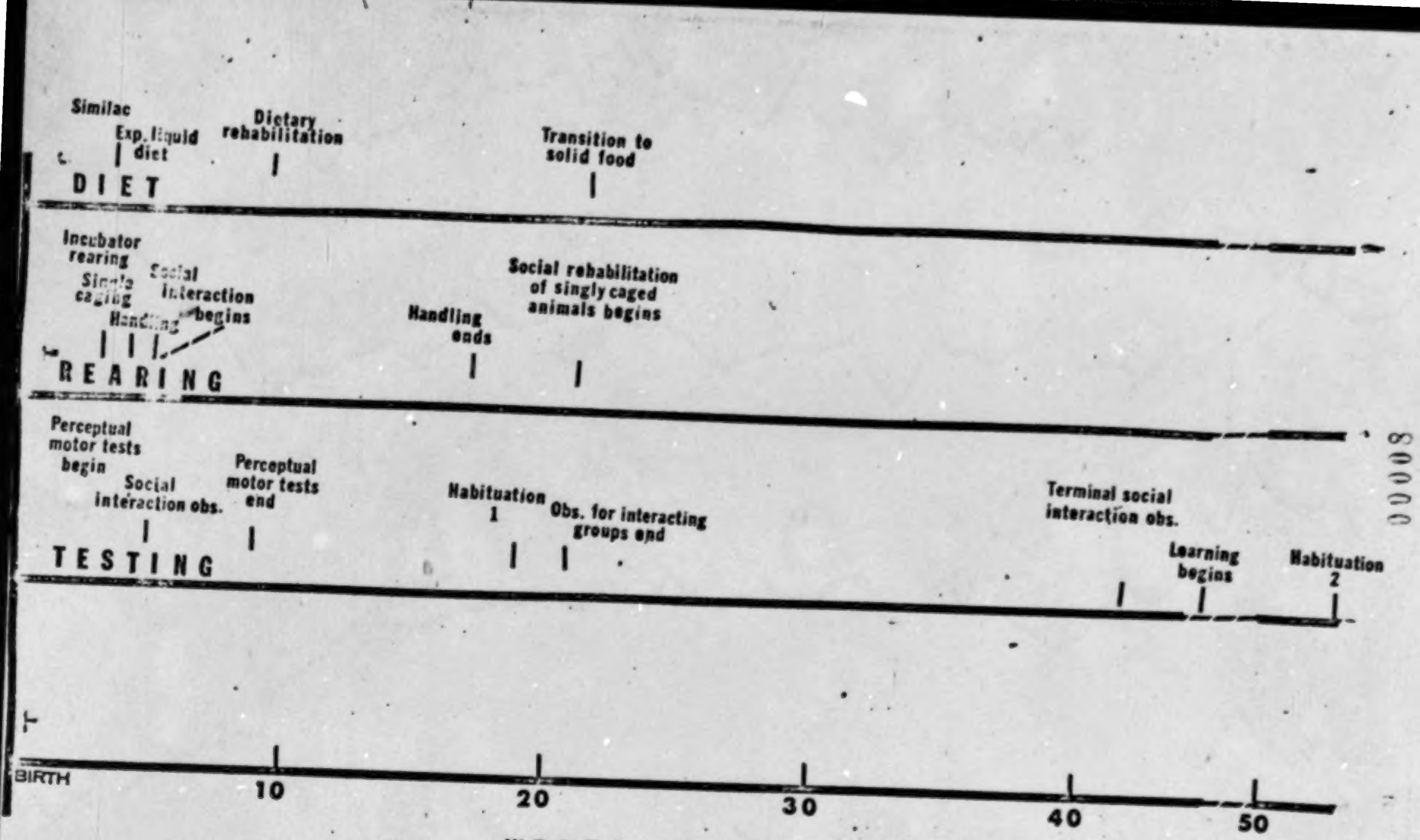
6 weeks. The time of deprivation was set as early as possible without markedly compromising the likelihood of survival. The squirrel monkey is born with a relatively large brain and the brain approaches adult size in a few weeks. Thus, very early nutritional deprivation is presumably required if it is expected to have a substantial impact upon brain development.

Group rearing conditions are provided by a satellite cage arrangement for each four animals--each living in a single cage with controlled access to a common playpen (slide-photograph). Each four social groups were allowed access to their playpens for 4 hours a day. Two of these groups received approximately 10 minutes daily of individual handling between 3 and 12 weeks.

All animals were on normal diets from 8 weeks onward and the animals reared in isolated cages from birth were exposed to group experiences starting at 20 weeks of age. This slide (flow chart) indicates the time scale of the independent conditions and the schedule of the observations and tests. The details of each observation and test will be described as the results obtained with these measures are presented.


SINGLY CAGED
NON-HANDLED INTERACTING
HANDLED INTERACTING
PROTEIN DEFICIENT 2-8 WEEKS OF AGE
N=4
N=4
N=4
DIET
N=4
N=4
N=4
CONTROL
REARING

00007



TIME LINE OF STUDY

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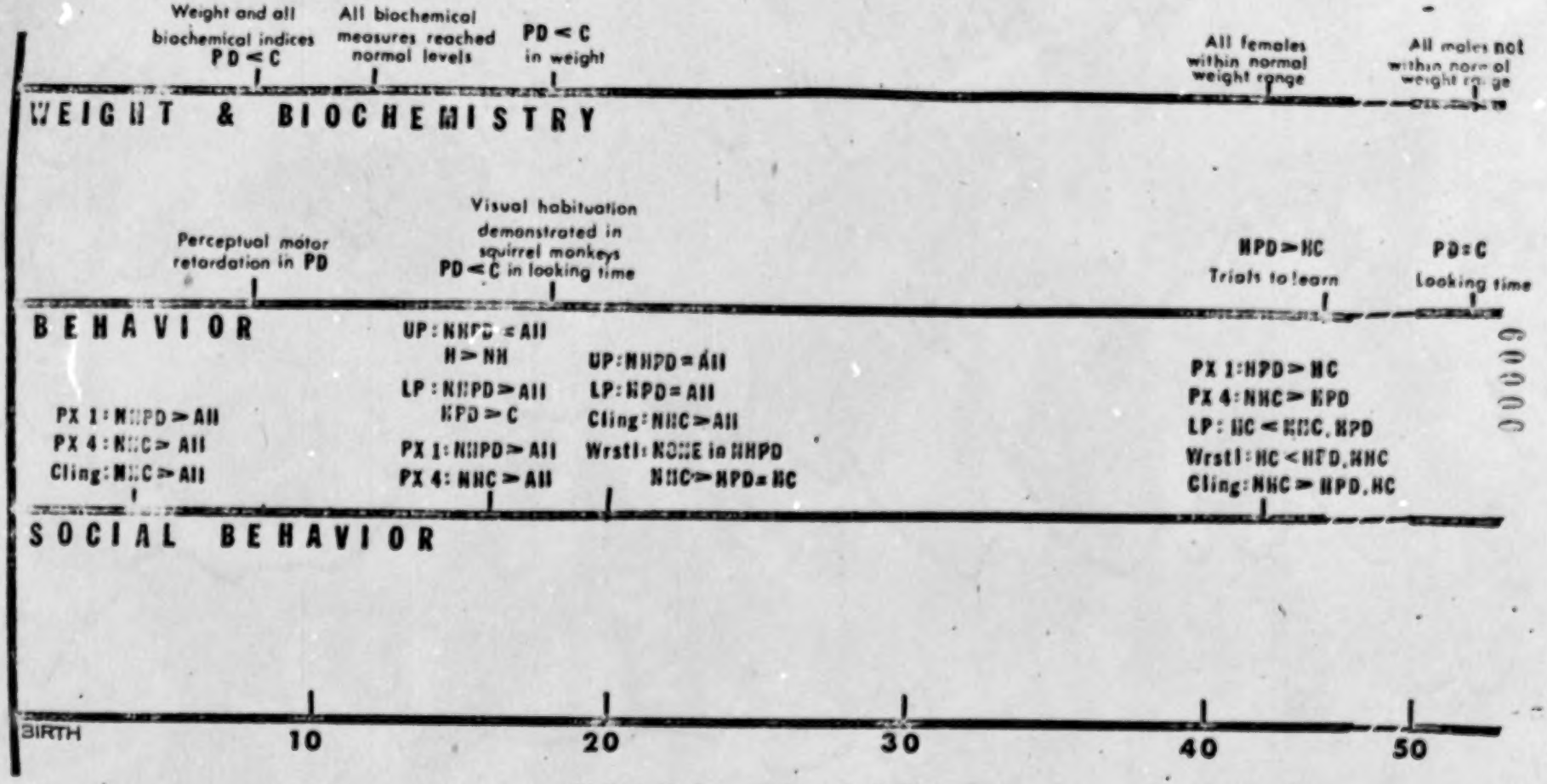
Weight and all biochemical indices PD < C
All biochemical measures reached normal levels
PD < C in weight
All females within normal weight range
All males not within normal weight range
WEIGHT & BIOCHEMISTRY
Perceptual motor retardation in PD
Visual habituation demonstrated in squirrel monkeys PD < C in looking time
HPD > HC Trials to learn
PD = C Looking time
BEHAVIOR
PX 1: NHPD > All
PX 4: NHC > All
Cling: NHC > All
UP: NHPD < All
H > NH
LP: NHPD > All
HPD > C
PX 1: NHPD > All
PX 4: NHC > All
UP: NHPD = All
LP: HPD = All
Cling: NHC > All
Wrstl: NONE in NHPD
NHC > HPD = HC
PX 1: HPD > HC
PX 4: NHC > HPD
LP: HC < NHC, HPD
Wrstl: HC < HPD, NHC
Cling: NHC > HPD, HC
SOCIAL BEHAVIOR
BIRTH
10
20
30
40
50
WEEKS OF AGE

TIME LINE OF STUDY

SUMMARY